DETAILED ACTION

Response to Amendment

1. Claims 46-66 have been cancelled, claims 67-71 newly added, as requested in the amendment filed on February 25, 2008. Following the amendment, claims 67-71 are pending and are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on February 25, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. As per amendments filed February 25, 2008, Claims 67-71 are rejected under 35 U.S.C. 101, as applied to Claims 46 and 65, for reasons of record in the Office action mailed October 25, 2007.

On pages 3-5 of Remarks filed February 25, 2008, Applicant traverses the rejection on the grounds that the Office has failed to establish a *prima facie* case because the Office "has provided no basis as to why one skilled in the art would not have accepted the asserted utility of the claimed polypeptide as a midkine antagonist in view of the teachings provided in the as-filed specification" (page 4, lines 5-7).

Applicants further argue that via sequence annotation of the structure of the claimed polypeptide, Applicant was able "to deduce specific and credible function", specifically, the proline rich tail of the claimed polypeptide "is suggested to interfere with receptor binding" (page 4, paragraph 2). Applicant concludes that "one skilled in the art would have reasonably believed, more likely than not, that the claimed polypeptide was capable of antagonizing midkine function" (lines bridging pages 4-5). While these arguments have been considered in full they are not found persuasive for the following reasons.

The pending claims have been reviewed in light of the revised Utility Guidelines published in the Federal Register and at 1242 Official Gazette 162, January 30, 2001.

The claims are directed to a composition of matter comprising an isolated polypeptide comprising an amino acid sequence of that recited in SEQ ID NO: 2. On pages 2-6, the specification states that based on a "high degree of sequence identity" as defined within the specification as "above about 20%-30% identity to other proteins in the same functional family", the polypeptide of the invention was identified as a variant of the midkine family of proteins. The specification asserts the following utilities: "may act as a dominant negative antagonist" (page 6, line 18); "may interfere with receptor binding" (Id, line 19); "may modulate (e.g. antagonize) swall/P21741/MK_HUMAN and that this ability may be due to the extended C-terminal tail of INSP0106" (page 7, lines 28-30); and "may be used in the treatment of disorders in which aberrant neurite growth promoting activity, neurite function, plasminogen activating activity, heparin binding activity, survival/differentiation of ES cell lines, regulation of embryonic development

and dentition are implicated". The specification variously teaches other asserted utilities for the polypeptide of the claims such as a tool for the identification of ligands (pages 33-36) or the production of antibodies (pages 18-20). Examiner maintains that the specification provides no evidence of either a highly conserved and well-characterized structural domain, nor of a well-established sequence annotation, that is indicative of a specific function of the claimed invention.

Furthermore, the specification lacks supporting evidence that the claimed invention possesses the asserted utility. Thus, the identification and reasonable confirmation of a "real world" context of use for the isolated polypeptide would require further experimentation. The specification states, "further experiments may now be performed ...[to] enable the continued investigation of the functional characteristics of the INSP106 polypeptides" (paragraph bridging pages 61-62), thus indicating that the functions of this polypeptide have yet to be characterized. Likewise, the disclosure states that "the identification of the function of the INSP106 allows for the design of screening methods ....ligands and compounds" (page 10 lines 20-24). The asserted function of the polypeptide is based upon sequence homology and annotation and the art generally acknowledges that function cannot be predicted based on structural similarity to a protein in the sequence databases (Skolnick et al. 2000, as cited in the previous Office action).

Therefore, the totality of the record continues to show that the asserted utility is neither specific nor substantial, and thus, the rejection based on lack of utility is maintained.

6. Claims 67-71 are also rejected under 35 U.S.C. 112, first paragraph, as applied to claims 46 and 65, for reasons of record in the previous Office Action. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

New Grounds of Rejection—Necessitated by Amendment

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. As currently amended, Claims 67-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 68-71 recite an isolated polypeptide comprising an amino acid sequence that has at least 90%, 95%, 98% or 99% sequence identity to SEQ ID NO:2 wherein said polypeptide is a midkine antagonist or antagonized the binding of midkine dimmers to protein tyrosine phosphatase ζ. The claims do not require that the polypeptides of

the claims possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of molecules that is defined only by at least 90% homology and by function. The instant specification fails to describe the entire genus of molecules that are at least 90% sequence identity to SEQ ID NO:2 and serve the functional requirements as encompassed by the claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of an isolated polypeptide as recited in SEQ ID NO:2. The claims, however, are drawn to polypeptides that are at least 90% homologous to SEQ ID NO:2, thus, the claims are not limited to specific molecules with known structure but rather the claims merely require the molecules that serve as a midkine antagonist or antagonize the binding of midkine dimmers to protein tyrosine phosphatase ζ.

To provide adequate written description and evidence of possession of a claimed genus of molecules, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is a recitation of homology and activity. There is not even identification of any particular portion of the structure that must be conserved for said activity. As stated above, it

would be unclear to one of ordinary skill in the art what molecules except SEQ ID NO: 2 meet the functional limitation of the claims. The specification does not provide a complete or even partial structural description of all of those molecules that are at least 90% homologous to SEQ ID NO: 2 and that maintain the activity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot discern the molecular structures encompassed by the genus of the claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of identifying specific activity. Adequate written description requires more than a mere recitation of activity as part of the invention and a reference to a potential method of isolating or screening. The compound itself is required. See *Fiers v Revel*, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. As currently amended, Claims 68 and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by PCT/US2002/029636, September 18, 2002, as cited in the previous office action.

Claims 68 and 69 are drawn to a an isolated polypeptide comprising an amino acid sequence at least 90% (claim 68) or at least 95% (claim 69) sequence identity to SEQ ID NO: 2.

PCT/US2002/029636 describes an isolated polypeptide specifically comprising an amino acid sequence that is 97.8% identical to SEQ ID NO: 2. The alignment is as follows:

Query Match 97.8%; Score 398; DB 7; Length 162;

Best Local Similarity 100.0%; Pred. No. 6.7e-39;
Matches 72; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 DCKYKFENWGACDGGTGTKVRQGTLKKARYNAQCQETIRVTKPCTPKTKAKAKGQRKEKG 60

Db 83 DCKYKFENWGACDGGTGTKVRQGTLKKARYNAQCQETIRVTKPCTPKTKAKAKGQRKEKG 142

Qy 61 VGLSRGAAPPPP 72

Db 143 VGLSRGAAPPPP 154

Therefore, the isolated polypeptide of PCT/US2002/029636 anticipates the composition of matter of the instant claims 68 and 69.

Conclusion

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M,W and ALT F 7 am to 3:30, T & R 5:30 -5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/Olga N. Chernyshev, Ph.D./
Primary Examiner, Art Unit 1649